

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 665045	FOR FURTHER ACTION <div style="text-align: right; font-size: small;">see Form PCT/ISA/220 as well as, where applicable, item 5 below.</div>	
International application No. PCT/JP2005/005601	International filing date (day/month/year) 18/03/2005	(Earliest) Priority Date (day/month/year) 18/03/2004
Applicant SUCAMPO AG		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 10 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ The international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. ☒ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. ☒ **Certain claims were found unsearchable** (See Box II).

3. ☒ **Unity of invention is lacking** (see Box III).

4. With regard to the **title**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regard to the **drawings**,

a. the figure of the **drawings** to be published with the abstract is Figure No. _____

☐ as suggested by the applicant.

☐ as selected by this Authority, because the applicant failed to suggest a figure.

☐ as selected by this Authority, because this figure better characterizes the invention.

b. ☒ none of the figures is to be published with the abstract.

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Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.b of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, the international search was carried out on the basis of:
 - a. type of material
 - ☒ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material
 - ☒ in written format
 - ☒ in computer readable form
 - c. time of filing/furnishing
 - ☐ contained in the international application as filed
 - ☐ filed together with the international application in computer readable form
 - ☒ furnished subsequently to this Authority for the purpose of search
2. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional comments:

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Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
see FURTHER INFORMATION sheet PCT/ISA/210
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1-24, 29-33 (all partially)

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-24, 29-33 (all partially)

Provision of a polymorphism associated with expression of the Endothelin 1 gene (coding/non-coding)

2. claims: 1-24, 29-33 (all partially)

Provision of a polymorphism associated with expression of the Endothelin Receptor A (coding/non-coding)

3. claims: 1-24, 29-33 (all partially)

Provision of a polymorphism associated with expression of the Endothelin Receptor B (coding/non-coding)

4. claims: 1-24, 29-33 (all partially)

Provision of a polymorphism associated with the Mitochondrial gene

5. claims: 1-24, 29-33 (all partially)

Provision of a polymorphism associated with Angiotensin II type 1 receptor gene promoter region

6. claims: 34, 35 and 1-24 (partially) 29-33 (partially)

Provision of a polymorphism associated with Angiotensin II type 2 receptor gene promoter region

7. claims: 1-24, 29-33 (all partially)

Provision of a polymorphism associated with the Paraoxonase 1 gene I

8. claims: 1-24, 29-33 (all partially)

Provision of a polymorphism associated with the Noelin 2 gene

9. claims: 1-24, 29-33 (all partially)

Provision of a polymorphism associated with the adrenergic receptor gene

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

10. claims: 1-24, 29-33 (all partially)

Provision of a polymorphism associated the Myocilin gene

11. claims: 1-24, 29-33 (all partially)

Provision of a polymorphism associated with Optineurin alone and combinations with the TNFalpha gene

12. claims: 1-24, 29-33 (all partially)

Provision of a polymorphism associated with expression of the E-Selectin gene

13. claims: 1-24, 29-33 (all partially)

Provision of a polymorphism associated the TP53 gene

14. claims: 1-24, 29-33 (all partially)

Provision of a polymorphism associated with the Microsomal epoxide hydrase 1 gene

15. claims: 1-24, 29-33 (all partially)

Provision of a polymorphism associated with Endothelin converting enzyme gene promoter region gene

16. claims: 1-24, 29-33 (all partially)

Provision of a polymorphism associated the Heatshock protein promoter region

17. claims: 1-24, 29-33 (all partially)

Provision of a polymorphism associated with CD95 gene promoter region gene

18. claims: 1-24, 29-33 (all partially)

Provision of a polymorphism associated with adrenergic receptor gene

19. claims: 25, 26

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Provision of an isolated polynucleotide disclosed in claim
25

20. claims: 27, 28

Provision of an isolated polynucleotide disclosed in claim
27

21. claims: 29, 30

Provision of an isolated polynucleotide disclosed in claim
28

FURTHER INFORMATION CONTINUED FROM PCT/SA/ 210

Continuation of Box II.1

Although claims 2-13 are directed to a diagnostic method practised on the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

Although claims 29-35 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

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A. CLASSIFICATION OF SUBJECT MATTER

C07K14/575 C12Q1/68

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

C07K C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, PAJ, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>BROWN MICHAEL D ET AL: "Phylogenetic analysis of Leber's hereditary optic neuropathy mitochondrial DNA's indicates multiple independent occurrences of the common mutations"</p> <p>HUMAN MUTATION, vol. 6, no. 4, 1995, pages 311-325, XP009054854 ISSN: 1059-7794 the whole document</p> <p style="text-align: center;">----- -/--</p>	



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

° Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *G* document member of the same patent family

Date of the actual completion of the international search

25 October 2005

Date of mailing of the international search report

03. 02. 2006

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>HOLLANDER D A ET AL: "OUTFLOW PATHWAY ANOMALIES ASSOCIATED WITH MULTIPLE CYP1B1 MUTATIONS IN CONGENITAL GLAUCOMA" ARVO ANNUAL MEETING ABSTRACT SEARCH AND PROGRAM PLANNER, vol. 2003, 2003, page Abstract No. 1117, XP009054897</p> <p>& ANNUAL MEETING OF THE ASSOCIATION FOR RESEARCH IN VISION AND OPHTHALMOLOGY; FORT LAUDERDALE, FL, USA; MAY 04-08, 2003 the whole document</p> <p>-----</p>	
A	<p>BU X ET AL: "X CHROMOSOME-LINKED AND MITOCHONDRIAL GENE CONTROL OF LEBER HEREDITARY OPTIC NEUROPATHY EVIDENCE FROM SEGREGATION ANALYSIS FOR DEPENDENCE ON X CHROMOSOME INACTIVATION" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, vol. 88, no. 18, 1991, pages 8198-8202, XP002347836</p> <p>ISSN: 0027-8424 the whole document</p> <p>-----</p>	
A	<p>CHINNERY P F ET AL: "The mitochondrial ND6 gene is a hot spot for mutations that cause Leber's hereditary optic neuropathy" BRAIN, vol. 124, no. 1, January 2001 (2001-01), pages 209-218, XP002347837</p> <p>ISSN: 0006-8950 the whole document</p> <p>-----</p>	
X	<p>WO 02/22881 A (DZGENES, LLC; MOSKOWITZ, DAVID, W) 21 March 2002 (2002-03-21) claims</p> <p>-----</p>	1-24, 29-33
X	<p>WO 02/24747 A (EPIDAUROS BIOTECHNOLOGIE AG; BRINKMANN, ULRICH; HOFFMEYER, SVEN) 28 March 2002 (2002-03-28) Abstractclaims</p> <p>-----</p>	1-24, 29-33

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Information on patent family members

International Application No

PCT/JP2005/005601

Patent document cited in search report		Publication date		Patent family member(s)		Publication date
WO 0222881	A	21-03-2002	AU	9455901 A		26-03-2002
WO 0224747	A	28-03-2002	AU	8986101 A		02-04-2002